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Elevated Levels of Soluble ICAM-1 in Serum of Patients With Acute Myeloid Leukemia Undergoing Bone Marrow Transplantation

Yasuhiro Maeda, Junichi Chihara, Fusanari Horiuchi, Jun-ichi Miyatake, Yoichi Tatsumi, Fumiaki Urase, Kiyohiro Irimajiri, Shigenori Nakajima, and Atsushi Horiuchi

Third Department of Internal Medicine (Y.M., F.H., J.-i.M., Y.T., F.U., K.I., A.H.) and Fourth Department of Internal Medicine (J.C., S.N.), Kinki University School of Medicine, 377-2, Ohno-Higashi, Osaka-Sayama, Osaka, Japan

Serum soluble ICAM-1 concentrations were measured in 10 patients with or without chronic graft-vs.-host disease (GVHD) after allogeneic bone marrow transplantation. The serum soluble ICAM-1 levels in the patients with chronic GVHD were significantly higher than that in the patients without chronic GVHD. The data indicated that serum soluble ICAM-1 is a useful parameter for predicting chronic GVHD. © 1996 Wiley-Liss, Inc.

Key words: serum soluble ICAM-1, BMT, AML patients, chronic GVHD

INTRODUCTION

It is known that intercellular adhesion molecule 1 (ICAM-1, CD54), a 90-kDa molecule homologous superfamily, is the principal ligand for leukocyte functional antigen 1 (LFA-1, CD11a/CD18) [1], and it has been suggested that evaluation of an 82-kDa soluble form of ICAM-1 (sICAM-1) might be useful for investigating and monitoring various inflammatory and immune disorders [2–4]. Elevated levels of sICAM-1 are also detectable in malignant disorders [5], including malignant melanoma [6], Hodgkin's disease [7], and chronic B-lymphocytic leukemia [8]. In this study, we measured sICAM-1 concentrations in serum samples from patients with acute myeloid leukemia (AML) before and after allogeneic bone marrow transplantation (BMT), using a sandwich enzyme-linked immunosorbent assay (ELISA).

PATIENTS AND METHODS

Ten patients with AML undergoing BMT were selected for this study. All patients were receiving marrow transplants from HLA-identical sibling donors. We divided these patients into two groups, A and B, characterized by the presence or absence of chronic graft-vs.-host disease (GVHD), respectively. Serum samples were collected from the patients once a week. The levels of sICAM-1 before BMT were measured after complete remission was achieved and before conditioning for BMT.

An ELISA kit (Bender Medsystems, Vienna, Austria) employing two antibodies to distinguish different epitopes of ICAM-1 molecules was used for the present assay. A 96-well plate was treated with anti-sICAM-1 (human) monoclonal antibody, and then 100 μl of the standard solution or the test sample was added, followed by 50 μl of horseradish peroxidase-labeled anti-sICAM-1 antibody. Then, the reaction was stopped using 4N sulfuric acid and the absorbance was determined at 450/620 nm using a Titertek Multiskan MCC/340 spectrophotometer (ICN Company, Costa Mesa, CA, USA). The sICAM-1 concentration in each sample was determined from a calibration curve.

RESULTS AND DISCUSSION

We compared the concentrations of sICAM-1 in patients before vs. after BMT. Normal individuals have low concentrations of sICAM-1 (range, 200 to 260 ng/ml). As shown in Table I, sICAM-1 in the serum of patients in group A increased significantly after BMT. In particular, the sICAM-1 level in patient no. 5, who had grade IV chronic GVHD, was greatly elevated after BMT. In

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Address reprint requests to Yasuhiro Maeda, M.D., Third Department of Internal Medicine, Kinki University School of Medicine, 377-2, Ohno-Higashi, Osaka-Sayama, Osaka, Japan 589.

TABLE I. Soluble ICAM-1 Levels in Clinical Course of Patients With AML Before and After BMT*

Group	Pt.	Type	sICAM-1 level (ng/ml) Before	10 days post-BMT	20 days	30 days	40 days	50 days	GVHD (grade)
A	1. MK	M2	229 ± 23	310 ± 123	300 ± 87	417 ± 102	635 ± 67	385 ± 46	+(II)
	2. KK	M1	337 ± 108	298 ± 32	370 ± 41	450 ± 88	542 ± 98	434 ± 112	+(II)
	3. NN	M3	198 ± 45	223 ± 88	255 ± 53	378 ± 102	560 ± 41	502 ± 68	+(I)
	4. KS	M2	245 ± 78	303 ± 86	335 ± 79	499 ± 65	598 ± 119	489 ± 65	+(II)
	5. MT	M1	567 ± 77	571 ± 113	589 ± 109	899 ± 114	1,010 ± 145	1,256 ± 123	+(IV)
B	6. YT	M4	188 ± 56	202 ± 56	267 ± 77	260 ± 98	302 ± 109	321 ± 79	–
	7. NT	M1	221 ± 66	234 ± 47	201 ± 123	265 ± 88	245 ± 66	255 ± 92	–
	8. SY	M2	261 ± 75	300 ± 63	278 ± 76	285 ± 29	242 ± 43	308 ± 84	–
	9. YY	M3	259 ± 75	295 ± 95	281 ± 90	228 ± 93	330 ± 82	312 ± 88	–
	10. NO	M2	278 ± 99	268 ± 58	309 ± 96	350 ± 112	282 ± 107	285 ± 50	–

*Soluble ICAM-1 in serum of patients with AML before and after BMT. These results represent the mean ± SD of three different experiments.

contrast, sICAM-1 in the serum of patients in group B was not significantly elevated. In our results, high sICAM-1 concentrations in serum were detectable before the development of chronic GVHD, indicating that this parameter is predictive of chronic GVHD. Indeed, about 2 weeks later, liver dysfunction associated with chronic GVHD was observed in all cases in our study. High concentrations of sICAM-1 in serum have been considered to result from an immune response or inflammation induced by chronic GVHD. We did not establish the mechanism of this phenomenon yet. Furthermore, it was reported that endothelial cells were activated during allogeneic BMT, mainly in acute GVHD [9], and Norton et al. [10] reported that a high expression of ICAM-1 on damaged bile duct epithelial cells was observed in chronic GVHD patients with liver dysfunction. These reports suggest that the high serum levels of sICAM-1 seen after BMT in this study might be derived from endothelial or epithelial cells. Thus, our findings suggested that monitoring sICAM-1 levels in serum might be useful for predicting chronic GVHD following BMT.

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